

What is claimed is:

1. An animal having a heterologous nucleic acid sequence replacing an allele of an *atonal*-associated nucleic acid sequence under conditions wherein said heterologous sequence inactivates said allele.
2. The animal of claim 1 wherein said heterologous nucleic acid sequence is expressed under the control of an *atonal*-associated regulatory sequence.
3. The animal of claim 1 wherein both *atonal*-associated alleles are replaced.
4. The animal of claim 3 wherein said heterologous nucleic acid sequences are nonidentical.
5. The animal of claim 3 wherein said animal has a detectable condition.
6. The animal of claim 5 wherein said detectable condition is selected from the group consisting of loss of hair cells, cerebellar granule neuron deficiencies, hearing impairment, an imbalance disorder, joint disease, osteoarthritis and abnormal proliferation of cells.
7. The animal of claim 1 wherein said heterologous nucleic acid sequence is a reporter sequence.
8. The animal of claim 1, wherein said *atonal*-associated allele is replaced with an *atonal*-associated nucleic acid sequence under the control of regulatable promoter sequence.
9. The animal of claim 1, wherein said *atonal*-associated allele is replaced with an *atonal*-associated nucleic acid sequence under the control of a tissue-specific promoter sequence.

10. The animal of claim 1 wherein said animal is selected from the group consisting of a mouse, *Drosophila*, zebrafish, frog, rat, hamster and guinea pig.
11. A method for screening for a compound in an animal wherein said compound affects expression of an *atonal*-associated nucleic acid sequence comprising:
- 5 delivering said compound to said animal, wherein said animal has at least one allele of an *atonal*-associated nucleic acid sequence inactivated by insertion of a heterologous nucleic acid sequence, wherein said heterologous nucleic acid sequence is under control of an *atonal*-associated regulatory sequence; and
- 10 monitoring for a change in said expression of said *atonal*-associated nucleic acid sequence.
12. The method of claim 11 wherein said compound affects expression of an *atonal*-associated nucleic acid sequence.
13. The method of claim 11 wherein said compound affects a detectable condition in
- 15 an animal.
14. The method of claim 11, wherein said heterologous nucleic acid sequence is a reporter sequence.
15. The method of claim 11, wherein said compound affects said detectable condition.
- 20 16. A method for screening for a compound in an animal, wherein said compound affects a detectable condition in said animal, comprising:
- delivering said compound to said animal wherein at least one allele of an *atonal*-associated nucleic acid sequence in said animal is inactivated by insertion

of a heterologous nucleic acid sequence, wherein said heterologous nucleic acid sequence is under the control of an *atonal*-associated regulatory sequence, and monitoring said animal for a change in the detectable condition.

17. The method of claim 16, wherein said delivery of said compound affects expression of said heterologous nucleic acid sequence.
18. The method of claim 16 wherein said compound affects said detectable condition.
19. The method of claim 16 wherein said compound affects expression of said heterologous nucleic acid sequence.
20. A method of treating an animal with a deficiency in cerebellar granule neurons or their precursors comprising delivery of a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.
21. The method of claim 20, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Math1.
22. The method of claim 20, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Hath1.
23. The method of claim 20, wherein said amino acid sequence or nucleic acid sequence is delivered by a delivery vehicle.
24. The method of claim 23 wherein said delivery vehicle is selected from the group consisting of an adenoviral vector, a retroviral vector, an adeno-associated viral vector, a plasmid, a liposome, a nucleic acid, a peptide, a lipid, a carbohydrate and a combination thereof.

25. The method of claim 23, wherein said delivery vehicle is selected from the group consisting of a viral vector or a non-viral vector.
26. The method of claim 23, wherein said delivery vehicle is a cell.
27. The method of claim 20, wherein said cell contains an alteration in an *atonal*-associated amino acid sequence.
28. The method of claim 20, wherein said amino acid sequence has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).
29. The method of claim 20, wherein said nucleic acid sequence encodes a polypeptide which has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).
30. A method of promoting mechanoreceptive cell growth in an animal, comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.
31. The method of claim 30, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Math1.
32. The method of claim 30, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Hath1.
33. The method of claim 30, wherein said amino acid sequence or nucleic acid sequence is administered by a delivery vehicle.
34. The method of claim 33 wherein said delivery vehicle is selected from the group consisting of an adenoviral vector, a retroviral vector, an adeno-associated viral

vector, a plasmid, a liposome, a nucleic acid, a peptide, a lipid, a carbohydrate and a combination thereof.

35. The method of claim 33, wherein said delivery vehicle is selected from the group consisting of a viral vector or a non-viral vector.

5 36. The method of claim 33, wherein said delivery vehicle is a cell.

37. The method of claim 30, wherein said cell contains an alteration in an *atonal*-associated nucleic acid sequence or amino acid sequence.

10 38. The method of claim 30, wherein said amino acid sequence has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).

39. The method of claim 30, wherein said nucleic acid sequence encodes a polypeptide which has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).

15 40. A method of generating hair cells comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.

41. The method of claim 40, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Math1.

20 42. The method of claim 40, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Hath1.

43. The method of claim 40 wherein said delivery comprises injecting into an inner ear a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence.

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- 44. The method of claim 40, wherein said amino acid sequence or nucleic acid sequence is administered by a delivery vehicle.
- 45. The method of claim 44 wherein said delivery vehicle is selected from the group consisting of an adenoviral vector, a retroviral vector, an adeno-associated viral vector, a plasmid, a liposome, a peptide, a nucleic acid, a lipid, a carbohydrate and a combination thereof.
- 46. The method of claim 44, wherein said delivery vehicle is selected from the group consisting of a viral vector or a non-viral vector.
- 47. The method of claim 44, wherein said delivery vehicle is a cell.
- 48. The method of claim 40, wherein said cell contains an alteration in an *atonal*-associated nucleic acid sequence or amino acid sequence.
- 49. The method of claim 40, wherein said amino acid sequence has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).
- 50. The method of claim 40, wherein said nucleic acid sequence encodes a polypeptide which has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).
- 51. A method of treating an animal for hearing impairment, comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.
- 52. The method of claim 51, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Math1.

53. The method of claim 51, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Hath1.
54. The method of claim 51 wherein said delivery comprises injecting into an inner ear a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence.
55. The method of claim 51, wherein said amino acid sequence or nucleic acid sequence is administered by a delivery vehicle.
56. The method of claim 55 wherein said delivery vehicle is selected from the group consisting of an adenoviral vector, a retroviral vector, an adeno-associated viral vector, a plasmid, a liposome, a nucleic acid, a peptide, a lipid, a carbohydrate and a combination thereof of said vectors.
57. The method of claim 55, wherein said delivery vehicle is selected from the group consisting of a viral vector or a non-viral vector.
58. The method of claim 55, wherein said delivery vehicle is a cell.
59. The method of claim 51, wherein said cell contains an alteration in an *atonal*-associated nucleic acid sequence or amino acid sequence.
60. The method of claim 51, wherein said amino acid sequence has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).
61. The method of claim 51, wherein said nucleic acid sequence encodes a polypeptide which has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).

62. A method of treating an animal for an imbalance disorder, comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.
63. The method of claim 62 wherein said delivery comprises injecting into an inner ear a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence.
64. The method of claim 62, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Math1.
65. The method of claim 62, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Hath1.
66. The method of claim 62, wherein said amino acid sequence or nucleic acid sequence is administered by a delivery vehicle.
67. The method of claim 66 wherein said delivery vehicle is selected from the group consisting of an adenoviral vector, a retroviral vector, an adeno-associated viral vector, a plasmid, a liposome, a nucleic acid, a peptide, a lipid, a carbohydrate and a combination thereof of said vectors.
68. The method of claim 66, wherein said delivery vehicle is selected from the group consisting of a viral vector or a non-viral vector.
69. The method of claim 66, wherein said delivery vehicle is a cell.
70. The method of claim 62, wherein said cell contains an alteration in an *atonal*-associated nucleic acid sequence or amino acid sequence.

71. The method of claim 62, wherein said amino acid sequence has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).
72. The method of claim 62, wherein said nucleic acid sequence encodes a polypeptide which has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).
73. A method of treating an animal for a joint disease comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.
74. The method of claim 73, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Math1.
75. The method of claim 73, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Hath1.
76. The method of claim 73 wherein said delivery comprises injecting into said joint a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence.
77. The method of claim 73 wherein said amino acid sequence or nucleic acid sequence is administered by a delivery vehicle.
78. The method of claim 77 wherein said delivery vehicle is selected from the group consisting of an adenoviral vector, a retroviral vector, an adeno-associated viral vector, a plasmid, a liposome, a nucleic acid sequence, a peptide, a lipid, a carbohydrate and a combination thereof.

79. The method of claim 77, wherein said delivery vehicle is selected from the group consisting of a viral vector or a non-viral vector.
80. The method of claim 77, wherein said delivery vehicle is a cell.
81. The method of claim 73, wherein said cell contains an alteration in an *atonal*-associated nucleic acid sequence or amino acid sequence.
- 5 82. The method of claim 73, wherein said amino acid sequence has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).
83. The method of claim 73, wherein said nucleic acid sequence encodes a polypeptide which has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).
- 10 84. The method of claim 73 wherein said joint disease is osteoarthritis.
85. A method of treating an animal for an abnormal proliferation of cells comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.
- 15 86. The method of claim 85, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Math1.
87. The method of claim 85; wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Hath1.
- 20 88. The method of claim 85 wherein said amino acid sequence or nucleic acid sequence is administered by a delivery vehicle.
89. The method of claim 88 wherein said delivery vehicle is selected from the group consisting of an adenoviral vector, a retroviral vector, an adeno-associated viral

vector, a plasmid, a liposome, a nucleic acid, a peptide, a lipid, a carbohydrate and a combination thereof.

90. The method of claim 88, wherein said delivery vehicle is selected from the group consisting of a viral vector or a non-viral vector.

5 91. The method of claim 88, wherein said delivery vehicle is a cell.

92. The method of claim 85, wherein said cell contains an alteration in an *atonal*-associated nucleic acid sequence or amino acid sequence.

93. The method of claim 85, wherein said amino acid sequence has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).

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94. The method of claim 85, wherein said nucleic acid sequence encodes a polypeptide which has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).

95. The method of claim 85, wherein said cell is a cancer cell.

15 96. A method of treating an animal for an abnormal proliferation of cells comprising altering *atonal*-associated nucleic acid sequence or amino acid sequence levels in a cell.

97. The method of claim 96, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Math1.

20 98. The method of claim 96, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Hath1.

99. The method of claim 96 wherein said *atonal*-associated nucleic acid sequence or amino acid sequence contains an alteration.

100. The method of claim 96, wherein said cell is a cancer cell.
101. A method of treating an animal for a disease that is a result of loss of functional *atonal*-associated nucleic acid or amino acid sequence comprising delivering a therapeutically effective amount of an *atonal*-associated amino acid sequence or nucleic acid sequence to a cell of said animal.
- 5 102. The method of claim 101, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Math1.
103. The method of claim 101, wherein said *atonal*-associated amino acid sequence or nucleic acid sequence is Hath1.
- 10 104. The method of claim 101 wherein said amino acid sequence or nucleic acid sequence is administered by a delivery vehicle.
105. The method of claim 104 wherein said delivery vehicle is selected from the group consisting of an adenoviral vector, a retroviral vector, an adeno-associated viral vector, a plasmid, a liposome, a protein, a lipid, a carbohydrate and a combination thereof of said vectors.
- 15 106. The method of claim 104, wherein said delivery vehicle is selected from the group consisting of a viral vector or a non-viral vector.
107. The method of claim 104, wherein said delivery vehicle is a cell.
108. The method of claim 101, wherein said cell contains an alteration in an *atonal*-associated nucleic acid sequence or amino acid sequence.
- 20 109. The method of claim 101, wherein said amino acid sequence has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).

110. The method of claim 101, wherein said nucleic acid sequence encodes a polypeptide which has at least about 80% identity to about 20 contiguous amino acid residues of SEQ ID NO:58 (Hath1).

111. The method of claim 101, wherein said cell is a cancer cell.

5 112. A composition comprising an *atonal*-associated amino acid sequence or nucleic acid sequence in combination with a delivery vehicle, wherein said delivery vehicle results in delivery of a therapeutically effective amount of *atonal*-associated nucleic acid sequence or amino acid sequence into a cell.

10 113. The composition of claim 112, wherein said delivery vehicle comprises a vector that expresses an *atonal*-associated nucleic acid sequence or amino acid sequence in an animal cell.

114. The composition of claim 113, wherein said vector is selected from the group consisting of a viral vector, a plasmid, a liposome, a protein, a lipid, a carbohydrate and a combination thereof of said vehicles.

15 115. The composition of claim 112, wherein said delivery vehicle is the receptor-binding domain of a bacterial toxin.

116. The composition of claim 112, wherein said *atonal*-associated nucleic acid sequence is operatively linked to nucleic acid sequence encoding a receptor-binding domain of a bacterial toxin.

20 117. The composition of claim 112 wherein said *atonal*-associated nucleic acid sequence is operatively linked to nucleic acid sequence encoding a protein transduction domain.

118. The composition of claim 112, wherein said *atonal*-associated nucleic acid sequence is *Hath1*.

119. The composition of claim 112, wherein said *atonal*-associated nucleic acid sequence is *Math1*.

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